

Diagnosis And Management Of Shock In The Emergency Department

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Abstract

Shock is a state of acute circulatory failure leading to decreased organ perfusion, with inadequate delivery of oxygenated blood to tissues and resultant end-organ dysfunction. The mechanisms that can result in shock are divided into 4 categories: (1) hypovolemic, (2) distributive, (3) cardiogenic, and (4) obstructive. While much is known regarding treatment of patients in shock, several controversies continue in the literature. Assessment begins with identifying the need for critical interventions such as intubation, mechanical ventilation, or obtaining vascular access. Prompt workup should be initiated with laboratory testing (especially of serum lactate levels) and imaging, as indicated. Determining the intravascular volume status of patients in shock is critical and aids in categorizing and informing treatment decisions. This issue reviews the 4 primary categories of shock as well as special categories, including shock in pregnancy, traumatic shock, septic shock, and cardiogenic shock in myocardial infarction. Adherence to evidence-based care of the specific causes of shock can optimize a patient's chances of surviving this life-threatening condition.

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CME Objectives

Upon completion of this article, you should be able to:

1. Analyze available clinical data to be able to distinguish between the distinct pathophysiologic mechanisms that cause shock.
2. Describe and apply the initial resuscitative and therapeutic steps in the management of a patient presenting with undifferentiated shock.
3. Compare and contrast focused therapeutic interventions for the distinct pathophysiologic categories of shock.
4. Discuss the evidence-based clinical approach to hemorrhagic shock due to trauma.

Prior to beginning this activity, see "Physician CME Information" on the back page.

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Case Presentation

You are working in the ED late one evening when an 82-year-old man is brought in by his son. His son reports that earlier today, his father had been in his usual state of health, but this evening he found his father confused, with labored breathing. On arrival, the patient has the following vital signs: temperature, 38°C; heart rate, 130 beats/min; blood pressure, 110/60 mm Hg; respiratory rate, 34 breaths/min; and oxygen saturation, 89% on room air. He is delirious and unable to answer questions. A focused physical examination demonstrates tachycardia without extra heart sounds or murmurs, right basilar crackles on lung auscultation, a benign abdomen, and 1+ lower extremity pitting edema. You establish intravenous access with a peripheral catheter and send basic labs. A further history obtained from the son reveals that his father has congestive heart failure with a low systolic ejection fraction, as well as a history of several prior myocardial infarctions that were treated with stent placement.

As you consider this case, you ask yourself whether this patient is in shock, and if he is, what are the specific causative pathophysiologic mechanisms? You review which diagnostic tests are indicated to assist with the differential diagnosis of shock and you consider options for the initial management of this patient.

Introduction

Shock is a state of acute cardiovascular or circulatory failure. It leads to decreased delivery of oxygenated blood to the body's organs and tissues or impaired oxygen utilization by peripheral tissues, resulting in end-organ dysfunction.¹ The physiologic mechanism of oxygen delivery to peripheral tissues (DO_2) is described in the formula in **Equation 1**.

Equation 1

$$DO_2 = (\text{cardiac output}) \times [(\text{hemoglobin concentration}) \times SaO_2 \times 1.39] + (PaO_2 \times 0.003)$$

Abbreviations: DO_2 , oxygen delivery; PaO_2 , partial oxygen pressure; SaO_2 , arterial oxygen saturation.

Blood pressure is not included in this formula; while shock is frequently associated with hypotension, patients may present with “cryptic shock” in which they have a blood pressure typically considered to be within normal ranges, yet they have pathophysiologic signs of shock (particularly early in their clinical course). Many patients in shock ultimately develop hypotension, but a high index of suspicion is necessary to identify patients with shock and normal blood pressures during their initial presentation.

Equation 2 demonstrates the influence that cardiac output has on blood pressure (as evidenced by mean arterial pressure). A mean arterial pressure that decreases below a critical threshold will result in decreased cardiac output and, thereby, decreased DO_2 .

Equation 2

$$MAP = CO \times SVR$$

Abbreviations: CO, cardiac output; MAP, mean arterial pressure; SVR, systemic vascular resistance.

As noted in **Equation 3**, cardiac output is determined by stroke volume and heart rate, and stroke volume is affected by preload, afterload, and contractility. The concept of preload influencing stroke volume (and thereby affecting cardiac output and DO_2) is a core physiologic aspect of the assessment and management of patients in shock.

Equation 3

$$CO = HR \times SV$$

Abbreviations: CO, cardiac output; HR, heart rate; SV, stroke volume.

Changes in preload, stroke volume, system vascular resistance, and cardiac output can result in impaired tissue and organ perfusion. The impaired delivery of oxygen to peripheral cells that occurs in shock results in a transition from aerobic to anaerobic cellular metabolism. Anaerobic metabolism generates lactate via metabolism of glucose to pyruvate, and lactate can be used as a surrogate marker for tissue hypoxemia and the severity of shock. Cells can engage in anaerobic metabolism for a limited time, but persistent cellular hypoxia results in cell death and tissue necrosis, leading to multiorgan system dysfunction and failure. The saturation of venous oxygen measured from central vessels (such as the superior vena cava), is another biochemical marker of peripheral oxygen uptake and can be used diagnostically to help with prognosis in the comprehensive assessment of patients presenting in shock.

The pathophysiologic mechanisms that can result in shock are divided into 4 separate (but potentially overlapping) categories: (1) hypovolemic, (2) distributive, (3) cardiogenic, and (4) obstructive.²

Definitive treatment for patients in shock depends on the specific etiology; however, this may not be immediately clear on initial presentation to the emergency department (ED). As with much of emergency medicine, the initiation of therapy and patient stabilization may occur simultaneously with evaluation. The goals in treating patients in shock are restoring adequate organ perfusion and oxygen delivery while considering/treating the possible cause(s) of shock.

In early shock, compensation occurs by modulation of cardiac output and vascular tone by the autonomic nervous system.¹ Carotid baroreceptors respond to decreased blood pressure by triggering increased sympathetic signaling. This autonomic nervous system-mediated sympathetic response

results in an increase in contractility and heart rate, thereby increasing cardiac output. (See Equation 1 and Table 1, page 3). In addition, increased sympathetic signaling results in alpha-1 receptor activation and systemic vascular resistance. This issue of *Emergency Medicine Practice* analyzes the pathophysiology of the 4 types of shock and provides best practice recommendations on the diagnosis and management in the ED.

Critical Appraisal Of The Literature

A literature search was performed using Ovid MEDLINE® and PubMed from 1950 to December 2013. Areas of focus were shock, emergency management of shock, and emergency diagnosis of shock. Specific searches were performed for types of shock including the terms: *hypovolemic, hemorrhagic, distributive, septic, neurogenic, anaphylactic, cardiogenic, obstructive, pulmonary embolism, and cardiac tamponade*. High-quality review articles were noted and provided the foundation for additional primary literature review. Over 300 articles were reviewed, which provided background for further literature review.

The Cochrane Database of Systematic Reviews and the National Guideline Clearinghouse (www.guideline.gov) were also consulted.

Literature from emergency medicine journals was assessed. Although studies from the critical care or intensive care literature do not necessarily include ED patients, clinical lessons from these studies are often reasonable to apply to the ED population. Studies from cardiology literature were also included.

Randomized controlled trials were included in this review whenever possible. Due to the acute nature of patients presenting to the ED in shock, randomization in the ED can be difficult, thereby limiting

Table 1. Categories Of Shock²

Category	Hemodynamics	Causes
Hypovolemic	↓ preload ↑ SVR ↓ CO	Hemorrhage, GI losses, third spacing, burns
Distributive	↓ preload ↓ SVR ↑/↓ CO	Sepsis, anaphylaxis, neurogenic shock, pancreatitis
Cardiogenic	↑ preload ↑ SVR ↓ CO	Myocardial infarction, symptomatic bradycardia, valvular disease, heart blocks, end-stage heart failure
Obstructive	↓ preload ↑ SVR ↓ CO	Pulmonary embolism, tension pneumothorax, pericardial tamponade

Abbreviations: CO, cardiac output; GI, gastrointestinal; SVR, systemic vascular resistance.

the availability of these studies. Randomized controlled trials are more prevalent in the critical care and cardiology literature. Where randomized controlled trials are not available, prospective observational studies and retrospective studies were used.

Pathophysiology

Patients in shock present to the ED in varying states of critical illness, depending upon their age and underlying medical conditions, as well as the etiology and the clinical and temporal progression of shock. An expedited approach to patients in shock can identify underlying etiology(ies) of shock as well as reveal causes of shock that require specific therapeutic interventions (such as early source control for septic shock).³ A prompt evaluation focusing on rapid diagnosis and empiric resuscitation, usually before the results of laboratory or imaging tests are available, is critical.

Considering the specific category of the patient's shock (eg, hypovolemic, distributive, cardiogenic, or obstructive) can assist emergency clinicians in generating appropriate differential diagnoses for the underlying etiology(ies) of shock and thereby help guide definitive treatment.⁴

Hypovolemic Shock

Hypovolemic shock occurs due to inappropriately low intravascular volume leading to decreased preload, decreased stroke volume, and decreased cardiac output.^{5,6} Hypovolemic shock can be due to decreased intravascular fluid or decreased blood volume.^{5,6} Decreased blood volume is due to hemorrhage. Severe hemorrhage, resulting in loss of circulating red blood cells, can result in decreased myocardial oxygen delivery, further decreasing cardiac output, with primary compensatory responses of autonomic nervous system-mediated increases in systemic vascular resistance.

Distributive Shock

Distributive shock is characterized by profound systemic vasodilation and is commonly associated with relative intravascular volume depletion. Management often involves addressing both distributive and hypovolemic pathophysiology.

Primary compensatory responses to decreased systemic vascular resistance in distributive shock include increased cardiac output, tachycardia, and hyperdynamic left ventricular systolic contraction.^{4,7} In addition, decreased systemic vascular resistance and increased venous capacitance results in decreased preload, compromising cardiac output despite increases in heart rate and contractility. Up to 40% of patients with distributive shock due to sepsis may develop a transient cardiomyopathy. The path of this process has not been fully elucidated.⁸ Cardio-

myopathy of sepsis is characterized by decreased left ventricular inotropy and decreased cardiac output.⁹ Cardiomyopathy is associated with a mortality rate as high as 70%.¹⁰

While septic shock is the most common cause of distributive shock, other processes can cause distributive pathophysiology, including anaphylaxis, adrenal insufficiency, transfusion reactions, and liver failure. Although neurogenic shock is pathophysiologically characterized as distributive shock, clinical management of neurogenic shock is distinct from other forms of distributive shock. Emergency clinicians should entertain a broad differential while evaluating patients with distributive pathophysiology to avoid prematurely concluding that sepsis is the diagnosis. Furthermore, it is important to emphasize that while shock is often divided into 4 categories, some conditions can produce overlapping manifestations of several categories of shock. Specifically, sepsis can present with characteristics of distributive, hypovolemic, and even cardiogenic shock.

Cardiogenic Shock

Cardiogenic shock is due to the failure of the left ventricle to generate adequate arterial flow to deliver oxygenated blood to peripheral tissues. Cardiogenic shock may be due to disruptions in stroke volume and/or heart rate. Failure of the left ventricle to generate adequate oxygen delivery may be due to processes such as right ventricle failure or valvular disease.¹¹ Pathophysiologic processes that can negatively affect stroke volume include aberrations in preload, afterload, and myocardial contractility. Myocardial infarction is the most common cause of cardiogenic shock, but there are many other causes. (See Table 2.) For more information on cardiogenic shock due to myocardial infarction, see the "Special Circumstances" section on page 14.

Abnormal heart rates can also cause cardiogenic shock. Bradyarrhythmias can result in a low cardiac output, and tachyarrhythmias can result in decreased preload due to decreased diastolic filling time (resulting in a critically compromised stroke volume and decreased cardiac output). The primary systemic compensatory response to decreased cardiac output is an autonomic nervous system-mediated increase in systemic vascular resistance. This increase in systemic vascular resistance causes the common finding of cold and clammy extremities in patients with cardiogenic shock.

Obstructive Shock

Obstructive shock results from either a critical decrease in preload or an increase in left ventricle outflow obstruction.^{2,12} Extracardiac processes that increase intrathoracic pressure can result in obstructive shock by decreasing cardiac compliance and interrupting venous return by compressing the infe-

rior or superior vena cava. Tension pneumothorax,¹³ herniation of abdominal contents into the thorax,¹⁴ and positive pressure ventilation¹⁵ are processes that result in decreased cardiac compliance and obstruction of the vena cava, decreased preload, and decreased cardiac output.

Extracardiac processes that cause right ventricle outflow obstruction include severe pulmonary hypertension¹⁶ and massive pulmonary embolism.¹⁷ Increased right ventricle obstruction causes decreased right ventricle stroke volume, decreased pulmonary arterial flow, decreased left ventricle preload, decreased left ventricle cardiac output, and decreased delivery of oxygenated blood to peripheral tissues.

Table 2. Etiologies Of Cardiogenic Shock¹¹

Decreased Stroke Volume

- **Acute Myocardial Infarction**
 - Right-sided infarct
 - Large left-sided infarct
 - Infarct in setting of existing disease
 - Mechanical complications of infarction
- **Mechanical Complications Of Infarction**
 - Acute mitral regurgitation due to papillary muscle rupture
 - Ventricular septal defect
 - Free wall rupture
- **Valvular Heart Disease**
 - Mitral stenosis or regurgitation
 - Aortic stenosis or regurgitation
- **Dilated Cardiomyopathy**
 - Ischemic
 - Viral/bacterial
 - Toxin-induced
 - Rheumatologic
 - Thyroid disease
 - Pheochromocytoma
 - Congenital
 - Peripartum
 - Sarcoidosis
- **Hypertrophic Cardiomyopathy**
- **Restrictive Cardiomyopathy**
- **Myocarditis**
- **Takotsubo Cardiomyopathy**
- **Atrial Myxoma**
- **Orthotopic Transplant Rejection**
- **Cardiac Trauma**
 - Blunt
 - Penetrating
- **Atrial Myxoma**
- **Orthotopic Transplant Rejection**

Abnormal Heart Rates

- **Bradyarrhythmias**
 - Sick sinus syndrome
 - Junctional bradycardia
 - Complete heart block
- **Tachyarrhythmias**
 - Atrial fibrillation/flutter
 - Reentrant atrial tachycardia
 - Ventricular tachycardia
 - Ventricular fibrillation

Emergency Department Evaluation

Initial Stabilization

Preliminary assessment in the ED begins with a primary survey to identify the need for critical interventions such as intubation, mechanical ventilation, or obtaining vascular access. Patients may need to be immediately intubated for refractory hypoxemia, hypoventilation, or the inability to protect their airway. Early intubation is reasonable in patients with poor projected clinical trajectories, such as those with declining mental status or impending respiratory failure. Benefits of early mechanical ventilation may include improved systemic oxygenation as well as a marked decrease in work of breathing, further reducing systemic oxygen consumption and improving oxygen debt.^{18,19}

Oxygen saturation should be checked immediately and continuously monitored. The chest should be auscultated, with specific attention paid to equal air movement and bilateral chest wall rise. Typically, patients in shock who do not require immediate intubation and mechanical ventilation are given supplemental oxygen, although the optimal oxygen concentration in patients with shock is unknown. Recent data have suggested that critically ill patients with myocardial infarction or return of spontaneous circulation after cardiac arrest have increased mortality with hyperoxia.²⁰⁻²² However, these findings have not been demonstrated in a broad population of patients presenting with shock.

Central pulses should be palpated upon arrival if the patient's blood pressure is unknown. Patients should be immediately placed on a cardiac monitor, and an automated blood pressure cuff should be used to frequently monitor their mean arterial pressure. Intravenous access should be obtained, preferably with 2 large-bore intravenous lines. Occasionally, patients in shock will require an urgent central venous line placement for vascular access to deliver medications or for volume resuscitation. Intraosseous line placement is a fast and viable central circulation access option in patients with difficult intravenous access. A 12-lead electrocardiogram may help identify the etiology of shock; in addition to demonstrating evidence of myocardial infarction, electrocardiogram can determine the location of the infarction and alert emergency clinicians to potential associated complications.²³

History

Obtaining history from patients in shock may be difficult or impossible due to altered mental status. Family, emergency medical service providers, or other sources may provide context. Prior medical history and medications may assist in determining the etiology of shock; special attention should be paid to the use of or dependence on steroids. Patients found

unconscious without a witness should be evaluated for the possibility of trauma contributing to or causing their shock. Trauma may also present as a complication secondary to other shock etiologies.

Physical Examination

As with a secondary survey in trauma patients, patients in shock should be rapidly, yet thoroughly, evaluated from head to toe. Emphasis should be placed on evaluating distal perfusion, gathering data regarding the type of shock, and narrowing the differential diagnosis for specific underlying etiologies. Cool extremities, indicating peripheral vasoconstriction, may be helpful in differentiating cardiogenic from vasodilatory shock in which warm extremities and bounding pulses may be present.²³ A study evaluating specific physical examination findings to evaluate causes of shock in 68 patients found that capillary refill and skin temperature had a sensitivity of 89% and specificity of 68% for diagnosing distributive shock.²⁴

Not all patients in shock will present with alterations that are immediately recognized during primary or secondary surveys. Patients may present with compensated shock with a normal physical examination and normal blood pressures.^{25,26} Additionally, patients may have atypical presentations due to contributions from medications (beta-blockers) and/or underlying medical conditions. A 2013 prospective observational study of patients in septic shock presenting to the ED found that patients with classic signs of shock (eg, altered mental status, respiratory distress, and hypotension) were more likely to receive resuscitation bundles and early antibiotics compared to patients with only a biochemical diagnosis of septic shock (eg, elevated lactate).²⁷ Although this study was underpowered to detect a mortality difference, it emphasized the need to maintain vigilance for occult shock.

Determining the intravascular volume status of patients in shock is critical, as appreciating the volume status aids in categorizing shock and informs early treatment decisions.²⁴ However, assessing volume status may be quite challenging, particularly early in a patient's presentation. Traditional markers of hypovolemia include tachycardia or hypotension, although supine hypotension and tachycardia are insensitive.^{28,29} Orthostatic vital signs have been found to be reliable only with a large-volume blood loss.²⁸ A meta-analysis of 10 studies of healthy volunteers who were phlebotomized demonstrated that an increase in pulse rate of ≥ 30 beats/min had a sensitivity of 97% and specificity of 98% in patients with large blood loss (630-1150 mL), but a sensitivity of only 22% in patients with moderate blood loss (450-630 mL).²⁸ A decrease in systolic blood pressure of > 20 mm Hg was of no additional clinical value. Additionally, assessing orthostatic vital signs in critically ill patients

may not be practical or logistically possible.

An estimation of jugular venous pressure has been advocated to evaluate for right atrial pressures,²⁴ but it is often technically difficult to perform. A study that compared jugular venous pressure (measured by cardiologists) to right atrial pressures (measured by a pulmonary arterial catheter) in 96 patients with significant cardiac disease found an elevation over the clavicle to be 65% sensitive and 85% specific for identifying abnormally high right atrial pressures.³⁰ Whether even these marginal results could be replicated in an ED with an undifferentiated population remains unknown.

Monitoring urine output may be a useful adjunct to the assessment of volume status, but requires placing a Foley catheter and longitudinal monitoring, lessening the utility in the acute setting.

Diagnostic Studies

Laboratory Studies

Initial laboratory studies for patients in shock include complete blood count, basic serum chemistries (including renal function), and other tests (liver function tests, lipase/amylase, cardiac biomarkers, etc) as indicated by the individual patient's circumstances. An arterial blood gas test can be useful to evaluate the patient's acid/base status, as well as oxygenation and ventilation; a venous blood gas test can provide general information regarding a patient's acid/base status but it does not provide accurate information regarding oxygenation. Relevant cultures should be obtained early in the diagnostic workup. Generally, blood cultures are appropriate in most patients with suspected infection; urine, cerebral spinal fluid, pleural, ascitic, and/or other fluid compartment cultures should be sent, as clinically indicated.

Anaerobic metabolism leads to the production of lactate. When the production of lactate overwhelms clearance mechanisms, the serum lactate concentration will rise, making lactate a particularly useful marker in the evaluation of patients in shock. Elevated initial lactate levels have been found to correlate with mortality in a variety of patient populations, including patients with sepsis and septic shock,³¹ trauma, and cardiac arrest. While a lactate of ≥ 4 mmol/L is definitely considered to be abnormally elevated,³²⁻³⁴ lactates levels of ≥ 2 mmol/L have also been associated with increased mortality.³² Serial lactate levels (and, specifically, the presence or absence of lactate clearance) have prognostic value in patients with septic shock.^{35,36}

Base Deficit

In addition to lactate concentration, the base deficit warrants specific mention. Base deficit refers to a decrease in the concentration of basic molecules,

primarily bicarbonate, in the blood typically due to metabolic acidosis, but it can be seen with respiratory alkalosis as well. While base deficit is associated with hypovolemia and impaired tissue perfusion, a base deficit does not accurately identify an elevated serum lactate concentration or shock.³⁷ However, worsening base deficit is associated with increasing morbidity. A retrospective trial of 16,305 trauma patients demonstrated that worsening base deficit was linearly associated with worsening injury severity score.³⁸ Base deficit can be affected by intravenous fluids; for example, providing a patient intravenous sodium bicarbonate can potentially correct a base deficit, as the serum bicarbonate level is used to calculate the base deficit.³⁹ Given these considerations, the base deficit may be a useful laboratory finding when it is present (as it may alert clinicians to the presence of a metabolic acidosis) but the absence of a base deficit does not rule out significant pathology.

Imaging

Ultrasound

Given the limits of the physical examination, ultrasound is increasingly used in the ED to assess the volume status of patients in shock,^{40,41} as well as to assist in developing differential diagnoses.

Several ultrasound methods have been proposed to determine whether right-sided filling pressures are elevated, normal, or decreased, including measuring the end-expiratory inferior vena cava diameter,⁴² inferior vena cava respiratory variation, internal jugular vein diameter,⁴³ or right ventricle diameter.⁴⁴ Although all measures have shown promise in some studies, they have been inconsistent.⁴⁵⁻⁴⁷ One study compared maximal inferior vena cava diameter, inferior vena cava inspiratory collapse, and the ratio of internal jugular vein height to width and found that maximal inferior vena cava diameter was better able to differentiate a central venous pressure < 10 mm Hg from a central venous pressure > 10 mm Hg versus the other 2 measures.⁴⁶ (See the section, "Goals Of Fluid Resuscitation" on page 8 for a discussion of the limitations of central venous pressure as a measure of volume status.) Another recent study of patients with clinical evidence of hypovolemia found that all inferior vena cava indices were significantly lower than euvolemic control patients, and that these indices increased with fluid challenge.⁴⁰

Emergency clinicians may use bedside cardiac ultrasound to assess whether the left ventricle ejection fraction is normal, increased, or depressed, which can assist with determining the etiology of shock.⁴⁸⁻⁵⁰ A key study published in 2002 found that among emergency clinicians trained in focused bedside cardiac ultrasound, the correlation coefficient between emergency clinicians' and cardiologists' estimations of ejection fraction (Pearson $r = 0.86$)

was similar to the correlation of the ejection fraction estimations between 2 different cardiologists reviewing the same cardiac ultrasounds.⁵¹ The main limitation of this tool is the additional training required for emergency clinicians.

Ultrasound may also be used to assess for abdominal aortic aneurysm (AAA). Although leaking or ruptured AAAs are often retroperitoneal (so free fluid is not seen on ultrasound), identifying an AAA can inform whether further evaluation is warranted to determine if it is a possible source of shock. A recent systematic review of 7 studies of ultrasound assessment for AAA in the ED found that the sensitivity of ED ultrasound for AAA was 99%, with a specificity of 98%.⁵²

Protocols for focused ultrasound evaluations for nontrauma hypotensive patients have been proposed, such as the Abdominal and Cardiac Evaluation with Sonography in Shock (ACES) protocol.⁵³ Another point-of-care multiorgan ultrasound protocol studied 108 patients with undifferentiated hypotension. Ultrasound views looked at cardiac function, inferior vena cava diameter and collapsibility, pulmonary congestion, consolidations and sliding, abdominal free fluid and AAA, and leg vein thrombosis, and found good concordance between ultrasound diagnoses and final diagnoses, with almost perfect concordance once 13 cases with an ultimately unclear diagnosis were excluded.⁴⁴

While ultrasound shows great promise in evaluating patients in shock, the literature suffers from inconsistent techniques and definitions, making comparison among studies difficult. Additionally, a major limitation of many studies is that they rely on healthy volunteers, which is a very different population from undifferentiated critically ill ED patients. While ultrasound will likely have an increasingly important role in assessing shock, as the best techniques and evidence-based use are delineated, for now, ultrasound should be considered a diagnostic adjunct to be used and interpreted with other clinical data.

Chest X-Ray

Chest x-ray can assist in diagnosis of the etiology of shock. Special attention is paid to the heart size, presence of edema, infiltrates or effusions, and free air.²³ While a chest x-ray can provide useful clinical data, it has limitations. For example, the absence of congestion on an initial chest x-ray does not exclude the diagnosis of acute decompensated heart failure.^{23,54} Furthermore, anteroposterior chest x-rays are particularly limited in that the posterior lungs are poorly visualized compared to posterior-anterior films.

Computed Tomography

Computed tomography (CT) is a generally accurate and noninvasive means of detecting internal pathol-

ogy from various infections, vascular processes, or trauma. While CT imaging can be performed relatively rapidly, patients must travel from the ED to the CT scanner, which may be hazardous for unstable patients in shock. The potential benefits of CT, including diagnosing the etiology of shock and facilitating attempts at source control, must be weighed against possible risks associated with travel. Since ultrasound is increasingly prevalent in the ED as a point-of-care radiographic tool, it may be a reasonable strategy to use it as a first-line radiographic assessment, followed by CT if ultrasound is unrevealing, acknowledging that it is less accurate than CT imaging.^{55,56} Ultimately, these recommendations must be modified to the clinical setting, as the decision to pursue CT and the prioritization and urgency of these studies will be directly informed by the facility and the patient's clinical circumstances.

Echocardiography

Formal echocardiography may be useful in patients for whom cardiogenic shock is suspected, and who are not taken immediately to the catheterization laboratory,^{57,58} or for patients with suspicion for aortic dissection⁵⁹ or pulmonary embolism.^{60,61} However, due to the time delays typically associated with formal echocardiography, it is generally not a component of the front-line evaluation of patients in shock presenting to the ED.

Other Diagnostics

Further diagnostic studies may also be indicated based on a patient's presentation. For example, lumbar puncture is indicated in patients with suspected meningitis after antibiotics have been administered; diagnostic paracentesis is indicated for patients with suspected spontaneous bacterial peritonitis; and magnetic resonance imaging is appropriate for suspected epidural abscesses.

Treatment

Cardiovascular Monitoring

Patients presenting with shock or suspected shock should immediately be placed on a noninvasive cardiac monitor with an automated noninvasive blood pressure cuff. Further interventions and monitoring will depend on the patient's clinical circumstances.

Fluid Resuscitation

Although the details of treatment largely depend on the suspected etiology and the classification of shock, aggressive resuscitation begins while data are collected and a differential is formulated. In many cases of shock, fluid resuscitation is the primary treatment to increase perfusion and oxygen delivery. Early, aggressive resuscitation of critically ill patients may reverse tissue hypoxia and improve outcomes,

while uncorrected hypovolemia may lead to worsening organ failure.⁶² However, overzealous fluid resuscitation has been associated with increased morbidity and mortality in critically ill patients.⁶²⁻⁶⁴

Goals Of Fluid Resuscitation

The goal of fluid resuscitation is to improve myocardial performance by restoring preload, and thereby increasing stroke volume and cardiac output. By the Frank-Starling principle, as preload increases, stroke volume increases if the patient is on the ascending limb of the Frank-Starling curve. Once the optimal preload is achieved, further fluid administration will not increase stroke volume and may even be harmful.⁶⁵ Patients with cardiogenic shock may not respond to fluid challenges due to already-elevated end-diastolic pressures and the flat Frank-Starling curve of the failing heart.¹⁹ Conversely, patients in distributive shock may also not respond, due to high venous capacitance and low arteriolar tone.

Central venous pressure has commonly been used to guide fluid management, based on an assumption that central venous pressure is an adequate indicator of right ventricle preload, and that patients with low central venous pressures are volume-depleted, while patients with elevated central venous pressures are volume-overloaded. In 2001, Rivers et al published the seminal trial of early goal-directed therapy (EGDT) for septic shock.³³ In their protocol, central venous pressure is a major resuscitation target, with a goal of 8 cm to 12 cm water. Since this trial, central venous pressure has been a recommended target, and was recently endorsed again by the Surviving Sepsis Campaign in the 2012 guidelines update.⁶⁶ Those in favor of measuring central venous pressure argue that not only does its initial measurement assist in developing a differential diagnosis, but continued central venous pressure measurements allow for assessment of responsiveness to fluid therapy. However, due to the complex physiology of critically ill patients, the correlation between the central venous pressure and right ventricle end-diastolic volume is poor. Furthermore, right ventricle end-diastolic volumes may not reflect a patient's position on the Frank-Starling curve and preload reserve.⁶² Numerous studies have demonstrated that, in various clinical settings, no relationship between the central venous pressure (or change in central venous pressure) and fluid responsiveness.^{62,67}

"Fluid-responsiveness" is a term used to describe the clinical probability that a patient will respond to volume resuscitation. This is achieved through increased stroke volume and cardiac output.⁶² Only approximately 50% of hypotensive patients are volume-responsive.⁶⁸ Passive leg raise has been advocated as a rapid, noninvasive, and easily reversible tool to assess volume responsiveness. Lifting a patient's legs

from a horizontal to vertical position uses gravity to transfer pooled lower extremity blood to the thorax, thereby increasing cardiac preload by means of an "autotransfusion."⁶² The passive leg raise should be used with a monitor of cardiac output to assess the volume responsiveness.

Noninvasive cardiac monitors have been used in the ED to measure cardiac output, though they have yet to be proven to change measured clinical outcomes. (See the section, "Controversies And Cutting Edge," on page 15.) A recent meta-analysis of 8 studies found that passive leg raise predicted fluid responsiveness as measured by an increase in descending aortic blood flow. The assessment was performed by transesophageal Doppler imaging in critically ill patients with a global area under the receiver operating characteristic curve of 0.95, indicating excellent sensitivity and specificity of these maneuvers in real-time clinical practice in the ED.⁶²

For intubated mechanically ventilated patients in the ED, another measure of volume responsiveness is the pulse-pressure variation (the difference between systolic and diastolic pressures). For mechanically ventilated patients, end-expiratory intrathoracic pressures will be lower than end-inspiratory pressures, such that preload will be higher at end-expiration as compared to inspiration. Changes in preload during the respiratory cycle affect cardiac output and pulse pressure more in patients who are preload-dependent. Therefore, preload-dependent patients will have a wider pulse pressure variation from end-expiration to inspiration. Clinically, the absence of pulse pressure variation is useful as it indicates that a patient is unlikely to be volume-responsive. Although the precise number is uncertain, wide variation in the pulse pressure (generally > 13%) has been found to be a marker of volume responsiveness when compared to invasive means of monitoring stroke volume or cardiac index.⁶⁷ However, a major limitation in measuring pulse pressure variation is that not all patients in shock in the ED will be mechanically ventilated or have an arterial line.

Fluid Selection

Crystalloid is typically indicated for the initial treatment of undifferentiated shock, although there is an emerging body of evidence that this may not be the best selection for trauma patients or patients with traumatic hemorrhagic shock. (See the "Special Circumstances" section on page 12.)

Evidence has not supported the use of colloids in acute resuscitation, as there has been no evidence of improved outcomes with its use.⁶⁹ A trial of nearly 7000 critically ill patients randomized to receive resuscitation with either 4% albumin or normal saline found no difference in organ failure or death.⁷⁰ While the Surviving Sepsis Campaign guidelines continue to recommend consideration of albumin for

patients with sepsis receiving large-volume resuscitation,⁶⁶ a recent Cochrane Review emphasized that there is no evidence to support this practice.⁶⁹

In a randomized controlled trial in which 804 patients with severe sepsis were randomized to receive hydroxyethyl starch 6% versus crystalloid, 22% of patients in the hydroxyethyl starch group required renal-replacement therapy as compared to 16% of patients in the crystalloid group ($P = .04$); 51% of patients who received hydroxyethyl starch died versus 43% who received crystalloid ($P = .03$).⁷¹ These data, which are consistent with observational studies and animal models, confirm that hydroxyethyl starch should not be used for volume resuscitation in patients in shock, especially septic shock.

Central Venous Lines

Some patients who present in shock will require urgent central venous line placement to deliver medications or facilitate volume resuscitation. While there are no absolute or universally accepted criteria mandating central venous line placement, commonly accepted indications include: (1) the need to provide vasopressors or other centrally administered medications, (2) to measure central venous pressure or central venous oxygen saturation (ScvO₂), or (3) in cases of inadequate peripheral venous access. If possible, central access above the diaphragm is preferable in order to more accurately measure central venous pressure.^{18,72} Although central venous pressure does not reliably reflect volume responsiveness and is not an evidence-based volume target, it may still assist in determining a patient's specific type of shock. Decreased central venous pressure may indicate insufficient venous return and is typical of hypovolemic or distributive shock. Elevated central venous pressure suggests cardiogenic shock or obstructive shock.

ScvO₂ can be obtained via a central venous line. A ScvO₂ < 70% indicates that the oxygen delivery is inadequate to meet the oxygen uptake in the tissues, either due to decreased cardiac output or low hemoglobin, or due to increased oxygen demand in peripheral tissues. (See Equation 1, page 2; and Equation 4.)

Equation 4 demonstrates that a decrease in ScvO₂ can be explained by any one or any combination of the following pathophysiologic mechanisms: (1) a decrease in arterial oxygen saturation (SaO₂), (2) a decrease in cardiac output, (3) a decrease in the hemoglobin concentration, and/or (4) an increase in systemic oxygen consumption (VO₂).

Equation 4

$$\text{ScvO}_2 = \text{SaO}_2 - (\text{VO}_2 / (\text{CO} \times [\text{hemoglobin}] \times 1.38))$$

Abbreviations: CO, cardiac output; ScvO₂, central venous oxygen saturation; VO₂, systemic oxygen consumption.

Additionally, increased ScvO₂ may indicate poor oxygen uptake by tissues, either due to microcirculatory or mitochondrial failure. In a secondary analysis of 4 prospective studies of 619 patients treated per the EGDT protocol, initial ScvO₂ values of 90% to 100% were associated with worse in-hospital mortality than those with values 71% to 89%, or normoxia. In evaluating the maximum ScvO₂ in the first 6 hours of resuscitation, patients with hypoxic or hyperoxic ScvO₂ values had increased mortality compared to patients with normoxic values.⁷³

While there are no prospective randomized trials demonstrating a unique causal relationship between central venous line placement and improved clinical outcomes, a retrospective study from 1998 to 2009 of over 200,000 patients demonstrated an association with improved mortality for patients with septic shock who received a central venous line early in their hospital course.⁷⁴ Of note, the incidence of central venous line use in this population was quite low, with only 5.7% of patients in 1998 and 19.2% of patients in 2009 receiving a central venous line within 24 hours of presentation.⁷⁵ These results indicate that early central venous line placement correlates with improved mortality in septic shock; however, causation cannot be confirmed from a retrospective study, as other interventions beyond early central line placement that have been introduced in the care of critically ill patients between 1998 and 2009 (such as early antibiotics, goal-directed volume resuscitation, and/or low tidal volume ventilation) could have also influenced these results.

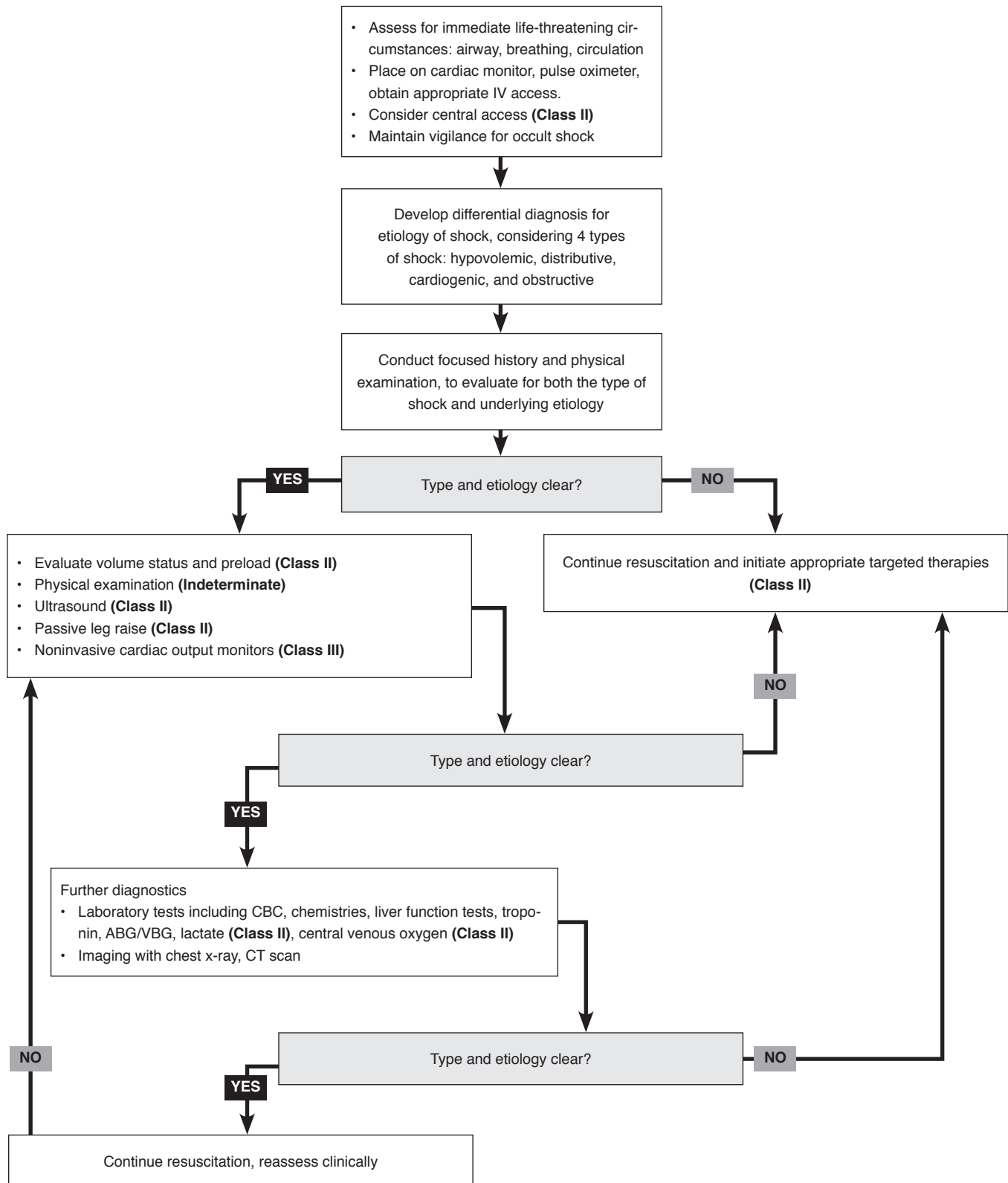
Arterial Lines

While recommended for the management of patients in shock, there are no prospective data indicating substantive differences in outcomes for patients treated with or without an arterial line. However, most clinicians prefer the close monitoring of both intra-arterial blood pressure monitoring and arterial blood gases in patients in shock. Emergency clinicians should be mindful of the limitations regarding interpreting arterial lines, particularly as they pertain to waveforms and physiologic phenomenon such as dampening or whip. As noted previously, an arterial line can be used to assess pulse pressure variation, which is a marker of volume responsiveness in hypotensive patients.⁶⁷

Pulmonary Artery Catheters

Although pulmonary artery catheters have been used for decades in the intensive care unit for invasive hemodynamic monitoring, their utility is debatable, as there have been no studies showing improved outcomes with their use. Furthermore, in a prospective randomized trial of 676 medical intensive care unit patients, pulmonary artery catheters demonstrated no advantage over standard central

Clinical Pathway For Diagnosing And Managing Shock



Abbreviations: ABG, arterial blood gas; CBC, complete blood count; CT, computed tomography; IV, intravenous; VBG, venous blood gas.
For class of evidence definitions, see page 11.

venous lines with regard to mortality and multiorgan failure.⁷⁵ There is no evidence supporting the use of pulmonary artery catheters in the immediate initial assessment of patients in shock in the ED.

Vasopressors

Once a patient is determined to be euvolemic, but there is still ineffective oxygen delivery, vasoactive medications are likely required. Various vasopressor medications may be used to support the mean arterial pressure by increasing systemic vascular resistance and/or cardiac output. While an in-depth discussion of vasopressors is beyond the scope of this review, norepinephrine is a strong alpha agonist with some beta-1 activity, and it is a recommended initial choice for most categories of shock, particularly when the etiology of shock is unknown.⁷⁶

Emerging data indicate that dopamine is associated with increased morbidity and potential mortality as compared to other first-line pressors. Specifically, a multicenter prospective trial of 1679 patients presenting with shock randomized patients to receive either dopamine or norepinephrine as the initial vasopressor.⁷⁶ There was no difference in mortality between patients receiving dopamine or norepinephrine, but patients receiving dopamine had a statistically significant higher incidence of arrhythmias.⁷⁶ Furthermore, a meta-analysis of 11 trials demonstrated a statistically significant increased risk of death associated with dopamine.⁷⁷ These results indicate that dopamine should not be used as a first-line pressor for patients in shock, including patients presenting with cardiogenic shock.

Clinical Course In The Emergency Department

If shock is identified early in the patient's presentation and prompt, focused, and appropriate care is provided, the patient's cardiovascular pathophysiology may improve and delivery of oxygenated blood to peripheral tissues may be restored. Lactate clearance can be helpful in determining response to

treatment for patients with severe sepsis or septic shock.^{35,36,76,78} One prospective study of 111 sequentially enrolled patients with sepsis presenting to the ED demonstrated that a decrease in lactate over the first 6 hours of treatment was associated with decreased mortality; specifically, mortality decreased by 11% for each 10% increase in lactate clearance.³⁵ Another randomized trial compared the monitoring with either ScvO₂ or lactate clearance of 300 patients presenting to the ED with severe sepsis or septic shock.⁷⁹ Lactate clearance of ≥ 10% was noninferior to achieving a ScvO₂ of at least 70% with regard to mortality.⁷⁹ These studies and others indicate that monitoring lactate clearance in the first 6 hours of treatment can provide information regarding response to initial treatments, as well as indicate the need for further interventions, including more aggressive volume resuscitation.^{31,36,80}

Ultrasound can demonstrate increased inferior vena cava diameter as a marker of adequate volume resuscitation, although it does not correlate with patients' overall systemic response to treatment.⁸¹ As such, inferior vena cava diameter is only one indication of response to treatment, as it specifically demonstrates a response to volume resuscitation, and it must be taken in the context of the entirety of a patient's clinical and laboratory data.

Deterioration

Even with early recognition, prompt resuscitation, and empiric treatment of shock, all patients presenting in shock are at risk for clinical worsening. Close monitoring is necessary to determine whether a patient is responding appropriately to treatment.

Patients in shock may have progressive, refractory vital sign abnormalities, usually manifested as progressive or refractory hypotension. While hypotension is not always present early in the presentation, it is almost always present in patients with progressive pathophysiology. A decreased mean arterial pressure despite targeted treatment indicates clinical deterioration.

Class Of Evidence Definitions

Each action in the clinical pathways section of *Emergency Medicine Practice* receives a score based on the following definitions.

Class I

- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:

- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II

- Safe, acceptable
- Probably useful

Level of Evidence:

- Generally higher levels of evidence
- Nonrandomized or retrospective studies: historic, cohort, or case control studies
- Less robust randomized controlled trials
- Results consistently positive

Class III

- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:

- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate

- Continuing area of research
- No recommendations until further research

Level of Evidence:

- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

This clinical pathway is intended to supplement, rather than substitute for, professional judgment and may be changed depending upon a patient's individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

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While specific clinical signs in refractory shock will depend on the underlying etiology(ies), general clinical considerations overlap all forms. Just as the assessment of airway and breathing is the first step in evaluating patients in shock, continued reassessment is critical. The progression of shock typically causes worsening metabolic acidosis, and patients may not be able to maintain adequate ventilation, particularly given impaired respiratory muscle function due to decreased delivery of oxygen, and decreased respiratory drive due to impaired cerebral perfusion. Additionally, patients may develop pulmonary edema from volume resuscitation, especially if further intravascular volume is given after they are no longer volume-responsive. Consequently, intubation and initiation of mechanical ventilation may be necessary for patients with progressive shock.

The intubation of a critically ill patient is a high-risk procedure, in that hypotensive and acidemic patients are at a higher risk of suffering acute hemodynamic collapse with endotracheal tube placement. This can occur due to vasodilation from induction medications, increased vagal tone from hypopharyngeal stimulation, and decreased right ventricle preload from positive-pressure ventilation. Ensuring that vasopressors are placed on pumps and in-line with intravenous fluids as well as providing empiric volume resuscitation peri-intubation may minimize the hemodynamic effects of intubation.

Patients who deteriorate despite initial resuscitation will likely require higher-level hemodynamic monitoring. Specifically, if a central venous line has not been placed, it is generally indicated for patients with progressive shock. Similarly, while studies have not demonstrated changes in clinical outcome attributable to arterial lines, they have been shown to be more precise in measuring mean arterial pressures in patients with hypotension.⁸² Therefore, arterial line placement is appropriate for patients with progressive shock. There is no role for pulmonary artery catheter placement for most patients with shock, and the utility of noninvasive hemodynamic monitors is uncertain. (See the "Controversies And Cutting Edge" section on page 15.)

Special Circumstances

Shock In Pregnancy

Pregnancy causes several maternal systemic and physiologic changes, including increased circulatory blood volume, decreased systemic vascular resistance, and increased cardiac output due to increases in both heart rate and stroke volume. The physiologic changes in pregnancy progress throughout gestation and are most prominent in the third trimester. Cardiac output can increase dramatically in normal pregnant women, increasing to up to 9 L/min immediately prepartum; however,

the decrease in systemic vascular resistance is more profound than the increase in cardiac output, and the net result is, typically, a modest reduction in mean arterial pressure of 5 mm Hg to 10 mm Hg from normal, prepregnancy levels. In this context, hemodynamic changes in a pregnant woman must be differentiated between normal physiologic responses versus pathologic processes.

Shock during pregnancy may be due to processes unrelated to pregnancy, such as the above-described obstructive, distributive, cardiogenic, and hypovolemic categories of shock. However, circulatory collapse may occur as a result of complications of pregnancy itself. Pregnancy-related complications that cause shock can be divided into either early or late complications.

The most common early complication is ectopic pregnancy with hemorrhage, resulting in hypovolemic shock. Emergency clinicians should have a high index of suspicion for ectopic pregnancy in women of child-bearing age presenting with abdominal pain and shock.

Late complications of pregnancy that may result in shock include peripartum pathologies such as pulmonary embolism,⁸³ amniotic fluid emboli,⁸⁴ uterine inversion or rupture,⁸⁵ postpartum hemorrhage, postpartum cardiomyopathy, and septic shock. Amniotic fluid embolism is thought to occur due to communication between placental and systemic veins or tears in the cervix or uterus in the setting of ruptured or damaged membranes. The precise mechanisms by which amniotic fluid causes systemic effects is unclear, but general consensus favors an anaphylactoid response in which amniotic fluid activates innate immunogenic responses, resulting in circulatory collapse and multiorgan system failure.⁸⁴

Given the complex physiology of pregnancy and the potential for additional disease processes that can result in shock, a comprehensive clinical approach is warranted to assess for complications both related and unrelated to pregnancy.

Traumatic Shock

The most common mechanism of shock following trauma is hypovolemia due to hemorrhage. The most important treatment for hemorrhagic shock is achieving hemostasis, also known as "source control." Resuscitation with medical interventions, such as transfusing blood products, is temporizing. As it takes time to mobilize resources to achieve hemostasis, a cogent approach to initial resuscitation is necessary.

In patients with trauma, there is compelling evidence suggesting that aggressive crystalloid resuscitation is associated with increased incidence of abdominal compartment syndrome, acute respiratory distress syndrome, nosocomial infections,

and death.⁸⁶⁻⁸⁹ Although some authorities advocate hypotensive resuscitation (goal systolic blood pressures of 80 mm Hg prior to definitive care^{19,90-92}) for hypotensive penetrating trauma patients without traumatic brain injury, data are conflicting and are primarily derived from animal studies,^{93,94} with only 2 human prospective randomized controlled trials.^{95,96} At this time, while hypotensive resuscitation may be a reasonable approach to patients with ongoing hemorrhage, definitive recommendations on optimal fluid resuscitation in these patients will require more data. Of note, hypotension in traumatic brain injury is associated with worse outcomes, and if traumatic brain injury is suspected, hypotension should always be avoided.⁹⁷

When clinically indicated, resuscitation with blood products (as opposed to crystalloid) is appropriate for management of hemorrhagic shock due to trauma. If emergency clinicians anticipate transfusing a significant volume of blood, a massive transfusion protocol may result in improved clinical outcomes.⁹⁸⁻¹⁰⁰ A massive transfusion protocol facilitates communication between the blood bank and the ED and results in efficient, ordered delivery of blood products. Coagulation factors can be rapidly diluted in patients with hemorrhage. Admin-

istration of packed red blood cells and crystalloid, with delay in administering fresh-frozen plasma, can further decrease serum concentrations of coagulation factors.¹⁰¹ A massive transfusion protocol will ensure that a reasonable ratio of fresh-frozen plasma and packed red blood cells and platelets are delivered to and transfused into the patient. While the precise ratio of fresh-frozen plasma to packed red blood cells that optimizes clinical outcomes is unknown, studies have demonstrated that a ratio of at least 1 unit of fresh-frozen plasma to 2 units of packed red blood cells is desirable.^{90,102,103} For a more detailed discussion on management of hemorrhagic shock, see the November 2011 issue of *Emergency Medicine Practice*, "Traumatic Hemorrhagic Shock: Advances In Fluid Management."

In addition to hypovolemic shock from hemorrhage, trauma patients are subject to all categories of shock, outlined in **Table 3**.

Septic Shock

In 2001, Rivers et al published a randomized controlled trial of an EGDT protocol for patients with sepsis.³³ This study of 263 patients with sepsis demonstrated an inhospital mortality of 30.5% in the EGDT group compared with 46.5% in the standard therapy group ($P = .009$). The goal of the protocol is to restore oxygen delivery to balance oxygen demand. The steps of the protocol are detailed in **Table 4**. There remains uncertainty among some clinicians regarding the clinical relevancy of this protocol overall and with regard to the relevant contribution of each individual component of the protocol. Several ongoing multicenter trials should provide more guidance regarding which aspects of the EGDT protocol are beneficial in clinical practice.

In addition to early volume resuscitation and initiation of vasopressors as clinically indicated, there

Table 3. Causes Of Shock In The Trauma Patient

Category/Causes of Shock	Diagnostic Tools
Hypovolemic <ul style="list-style-type: none"> • Hemorrhage • Hemothorax, hemoperitoneum, long-bone fracture, pelvic fracture, retroperitoneal bleed 	Physical examination <ul style="list-style-type: none"> • Bilateral breath sounds, abdominal examination, pelvic stability, extremity and back examinations FAST examination Imaging as indicated and tolerated
Distributive <ul style="list-style-type: none"> • Neurogenic shock • Fat emboli syndrome • SIRS due to hemorrhage 	Physical examination <ul style="list-style-type: none"> • Extremity strength, spine step-offs, rectal tone • Long bone or pelvic deformities
Cardiogenic <ul style="list-style-type: none"> • Cardiac contusion 	Bedside cardiac ultrasound ECG Troponin
Obstructive <ul style="list-style-type: none"> • Tension pneumothorax • Cardiac tamponade • Traumatic diaphragmatic hernia 	Physical examination <ul style="list-style-type: none"> • Bilateral breath sounds, heart sounds Thoracic ultrasound for lung sliding FAST examination

Note: Medical conditions may precipitate trauma.

Abbreviations: ECG, electrocardiogram; SIRS, systemic inflammatory response syndrome; FAST, focused assessment with sonography for trauma.

Table 4. Early Goal-Directed Therapy Protocol For Patients With Severe Sepsis And Septic Shock³³

1. Identify patients with SIRS criteria and SBP < 90 mm Hg or lactate \geq 4 mmol/L despite a crystalloid fluid challenge of 20 to 30 mL/kg over a 30-minute period.
2. Place central venous catheter.
3. Provide 500 mL of crystalloid boluses every 30 minutes until the central venous pressure is 8-12 mm Hg.
4. If mean arterial pressure is < 65 mm Hg, begin vasopressors.
5. If ScvO₂ is < 70%, then transfuse pRBCs to achieve a hematocrit of 30%.
6. If ScvO₂ is still < 70% after achieving a hematocrit of 30%, then begin dobutamine (starting at 2.5 mcg/kg).

Abbreviations: pRBCs, packed red blood cells; SBP, systolic blood pressure; ScvO₂, central venous oxygen saturation; SIRS, systemic inflammatory response syndrome.

is broad consensus that early administration of broad-spectrum antibiotics is warranted for patients presenting with septic shock. The studies supporting this clinical practice are retrospective; there are no randomized controlled trials assessing the timing of antibiotics in sepsis or septic shock.^{104,105} Nonetheless, because the available retrospective studies indicate that early administration of antibiotics is associated with improved clinical outcomes,^{104,105} including decreased mortality, current consensus guidelines strongly endorse immediately administering antibiotics when sepsis is considered as a diagnosis in patients in shock.¹⁰⁶

Early and appropriately broad antibiotic administration should parallel clinical evaluation for the source of the patient's infection. Whenever possible, source control should be achieved. Specific examples of source control include prompt removal of an infected indwelling catheter, abscess drainage, or treatment of an obstruction (eg, removal of a ureteral kidney stone or extraction of a gallstone in the common bile duct). Without source control, antibiotics may be insufficient, and patients will clinically deteriorate due to persistent systemic inflammation and progressive shock.

In 2004, the first set of Surviving Sepsis Campaign guidelines were published, with subsequent updates in 2008¹⁰⁶ and 2012.⁶⁶ The Surviving Sepsis Campaign has published the Surviving Sepsis Care Bundle, which encompasses a core set of clinical practices and interventions that should be performed simultaneously within a set time frame for a patient presenting with suspected sepsis or septic shock. The Surviving Sepsis Campaign 2012 sepsis bundles advise that within the first 3 hours patients have a lactate level checked, blood cultures drawn prior to antibiotics, broad-spectrum antibiotics given, and 30 mL/kg of crystalloid given for hypotension or lactate ≥ 4 mmol/L. Within 6 hours, vasopressors should be started for hypotension that does not respond to fluid resuscitation to maintain a mean arterial pressure ≥ 65 mm Hg. In the event of persistent hypotension despite volume resuscitation or initial lactate ≥ 4 mmol/L, measure central venous pressure with a goal of ≥ 8 mm Hg, check ScvO₂ for a goal of $\geq 70\%$, and remeasure lactate if initial lactate was elevated, with a goal of normalization.⁶⁶

Anaphylactic Shock

Anaphylaxis can result in shock due to a mixed distributive and hypovolemic pathophysiology. Anaphylaxis results from activation of mast cells and basophils through immunoglobulin E binding a specific allergen, resulting in the release of immunostimulatory and vasoactive proteins, with profound systemic vasodilation and diffuse vascular leak.¹⁰⁷ Vasodilation results in decreased systemic vascular resistance and mean arterial pressure (distributive

pathophysiology), and a vascular leak results in extravasation of intravascular fluid and decreased preload (hypovolemic pathophysiology.)

Volume resuscitation is appropriate in anaphylactic shock, but the mainstay of treatment is rapid administration of epinephrine. Epinephrine should be administered immediately if anaphylaxis is suspected. Epinephrine should be given intramuscularly if intravenous access is not available; treatment should not be delayed by attempting to place an intravenous line. The standard intramuscular dose of epinephrine is 0.3 mg to 0.5 mg in a 1:1000 dilution, and dosing may be repeated every 3 to 5 minutes as clinically indicated.

Histamine receptor antagonists (H1 and H2 blockers) and glucocorticoids are also recommended for patients with anaphylactic shock, although there are no studies demonstrating the clinical effects of these interventions.¹⁰⁸ In the absence of data guiding clinical practice, however, consensus recommendations endorse their use for anaphylaxis and anaphylactic shock.¹⁰⁹

Cardiogenic Shock Due To Myocardial Infarction

While cardiogenic shock can result from a variety of pathophysiologic processes that affect either stroke volume or heart rate, the most common cause of cardiogenic shock is myocardial infarction. Early recognition of acute coronary syndromes and myocardial infarction is critical, as delaying treatment and revascularization can result in significantly increased morbidity and mortality. In addition to aspirin and a continuous infusion of heparin, mobilization of the resources and personnel to achieve revascularization is critical. The seminal Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial demonstrated that early revascularization of patients presenting with cardiogenic shock due to myocardial infarction resulted in a statistically significant decrease in mortality at 6 months.¹¹⁰ When possible, percutaneous coronary intervention is preferable to fibrinolytic revascularization.¹¹¹ However, if percutaneous coronary intervention is not available within 90 minutes, then fibrinolytic therapy is preferable to medical management without revascularization.^{110,112}

For patients with refractory cardiogenic shock, intra-aortic balloon pumps have historically been used for mechanical cardiocirculatory support. Intra-aortic balloon pumps are placed through a femoral artery and inflate in the abdominal aorta during diastole and deflate during systole. This results in decreased left ventricle afterload and increased coronary perfusion during diastole, ideally decreasing myocardial oxygen demand and optimizing oxygen delivery. The utility of intra-aortic balloon pumps has recently been questioned, as a randomized con-

trolled trial of 600 patients with cardiogenic shock due to acute myocardial infarction demonstrated no difference in mortality between patients randomized to intra-aortic balloon pump versus no intra-aortic balloon pump.¹¹³ While intra-aortic balloon pumps may still provide benefit for selected patients with cardiogenic shock, this study demonstrates that many patients may be managed with revascularization and medical treatment alone.

Vasopressors may be necessary for hemodynamic support in patients with cardiogenic shock. Even if the decision is made to use an intra-aortic balloon pump, vasopressor support may be necessary to bridge a patient until an intra-aortic balloon pump is placed. While an in-depth discussion regarding vasopressor and inotrope selection is beyond the scope of this review, norepinephrine and/or dobutamine may be reasonable initial agents,¹¹³ although specific medication choices will be informed by the patient's clinical circumstances. Avoidance of dopamine is recommended in cardiogenic shock given an increased risk of tachyarrhythmias and, possibly, mortality.^{76,77}

Controversies And Cutting Edge

Early Goal-Directed Therapy

Despite the significant mortality difference in the EGDT trial,³³ the study and the details of the protocol have come into question over the last decade. Methodological criticisms range from the relatively small sample size, the high mortality in both arms,^{33,114,115} the fact that it was conducted at a single institution, and concerns about patients being excluded after enrollment.¹¹⁴

Additionally, many individual components of the protocol are not independently supported by high-quality data. The central venous pressure goal of 8 mm Hg to 12 mm Hg is the primary step in EGDT, although central venous pressure has repeatedly been shown to be a poor predictor of intravascular volume and fluid responsiveness.¹¹⁶

Furthermore, ScvO₂ is closely monitored in the EGDT protocol, but there are no data that show that following ScvO₂ improves outcomes over following lactate clearance,⁷⁹ and ScvO₂ alone does not necessarily correlate with mortality.¹¹⁷ As noted previously, an elevation in ScvO₂ may not only reflect improved oxygen delivery, but may also indicate poor oxygen utilization by the tissues.⁷³

This EGDT protocol called for blood transfusion for persistently low ScvO₂ if the patient had a hematocrit of < 30%. However, no other randomized trial has ever demonstrated improved outcomes with blood transfusion.^{118,119} As blood transfusions have been associated with increased risk of infections, respiratory failure, and death, the optimal approach to blood transfusion in sepsis is unknown.¹¹⁶ A recent

retrospective ED study found that packed red blood cell transfusion did not increase ScvO₂ or improve outcomes regarding organ failure.¹²⁰

Nonetheless, the EGDT trial did result in improved mortality in patients in septic shock with a 16% absolute risk reduction, and the protocol continues to receive much support.^{66,121-123} The EGDT trial remains the only completed randomized controlled trial of a resuscitation protocol/bundle in septic shock. Rivers et al noted that, historically, the mortality rate of septic shock was > 50%, and even the control arm in his study was treated with aggressive interventions that were beyond the standard of care at the time of the study.¹²³ However, a key difference between the groups was that while they received the same amount of total fluid, the treatment group received more fluid within the first 6 hours, whereas the conventional treatment arm received fluids later in their course.^{33,123} Early, aggressive, and multimodal bundled resuscitative interventions likely prevent the progression of septic shock and improves outcomes.¹²⁴

Three large randomized trials, The Australian Resuscitation in Sepsis Evaluation (ARISE), the Protocolized Care for Early Septic Shock in the United States (ProCESS), and the Protocolised Management in Sepsis in the United Kingdom (ProMISe), were completed in December 2013. Data from these multicenter studies will provide valuable information regarding the evolution of the role for EGDT and bundled care for patients with severe sepsis and septic shock.¹¹⁶

Pulmonary Embolism

Pulmonary embolism can cause shock due to extracardiac obstruction, resulting in a precipitous drop in cardiac output and impaired delivery of oxygen to peripheral tissues. While the role of thrombolysis in submassive pulmonary embolism is uncertain,¹²⁵ thrombolytics are indicated for massive pulmonary embolism resulting in shock. The data for thrombolysis in massive pulmonary embolism are limited, however, and only very small trials have been reported in the literature. One randomized prospective trial of 8 patients presenting with massive pulmonary embolism and shock demonstrated 100% survival of 4 patients treated with streptokinase as compared to 0% survival in patients treated only with heparin.¹²⁶ While the risk of hemorrhage from thrombolytic therapy is not insignificant, in the context of limited treatment options for massive pulmonary embolism, the potential benefits of thrombolysis for patients with shock due to pulmonary embolism probably outweigh the risks.

Noninvasive Hemodynamic Monitors

There are increasingly varied options for noninvasive hemodynamic monitoring in critically ill pa-

tients, including patients in shock.¹²⁷ Despite a variety of noninvasive hemodynamic and cardiac output monitoring devices, however, none have been found to improve clinical outcomes.^{127,128} Furthermore, the bulk of the available literature focuses on either validation of an individual noninvasive monitoring device with a gold standard or comparing the accuracy of one noninvasive monitoring device with another.¹²⁷ Examples of available noninvasive cardiac output monitoring devices include thoracic or whole-body bioimpedance monitors to estimate red blood cell mass changes during left ventricular systole, partial rebreathing of carbon dioxide to calculate the Fick equation, ultrasonographic monitoring (transthoracic or esophageal), and arterial and venous pulse oximetry/plethysmography variation.^{126,128-130} While potentially promising as noninvasive means of monitoring cardiac output and providing information regarding the nature of a

patient's shock, further studies with clinical outcome data are needed to guide the use of these monitoring devices in the diagnosis and management of patients with shock.

Disposition

After diagnosing the type and cause(s) of shock, patients in shock who promptly respond to treatment (including source control as clinically indicated) who do not require continuous vasopressor infusions or other resource-intensive interventions (such as intubation or high-level nursing care) may be appropriate for admission to a general floor, likely with continuous telemetry monitoring. Intensive care unit admission may be appropriate as well, particularly if there is uncertainty regarding the durability of the patient's response to initial treatment. It is unlikely

Pitfalls To Avoid In The Diagnosis And Management Of Shock

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1. **"His blood pressure is normal. He can't be in shock."**
Focusing on blood pressure alone as an indicator of shock can lead to missing signs of occult shock. Impaired organ perfusion, as evidenced by acute renal failure, altered mental status and/or increased serum lactate concentration, is a sign of shock pathophysiology and obligates early, aggressive clinical management.
2. **"Let's get the chest CT scan before deciding whether to give antibiotics or not."**
Failure to give antibiotics within 1 hour of presentation for all cases of possible septic shock may result in increased mortality. Early empiric antibiotic coverage is indicated for suspected septic shock with a target of administering (not just ordering) antibiotics within 1 hour of presentation.
3. **"Her ejection fraction is 30%, so let's start norepinephrine instead of giving a second liter of fluid."**
Adequate volume resuscitation for hypovolemic patients is critical. Markers of tissue perfusion such as lactate clearance, ScvO₂, pulse pressure variation with passive leg raise, and ultrasonographic measures of intravascular volume are appropriate determinants of the need for further volume resuscitation. A history of a low ejection fraction or other hypothetical concerns may lead clinicians to underresuscitate hypovolemic patients and may result in inappropriate initiation of vasopressors.

4. **"It could be a myocardial infarction, but let's wait for the troponin to come back before calling cardiology."**
Time-to-revascularization is one of the primary determinants of survival in patients with cardiogenic shock due to acute coronary syndromes. Delaying time to catheterization and revascularization will increase patient morbidity and mortality. When cardiogenic shock is possible, early consultation with cardiology and activation of the catheterization laboratory are necessary to optimize patient outcomes.
5. **"Let's give a fifth liter of saline and see if her mean arterial pressure comes up to at least 60 mm Hg..."**
Starting vasopressors without adequately volume resuscitating a patient while following markers of tissue perfusion and intravascular volume status is inappropriate (see pitfall #3); however, not recognizing that vasopressors need to be started for patients who are not volume responsive is also inappropriate. Patients with a pathologically decreased systemic vascular resistance may require vasopressors to maintain mean arterial pressure even after volume resuscitation and normalization of intravascular volume status. Continuing to administer fluids and not recognizing the need for vasopressors can result in perpetuating complications of shock.

that a patient who presents to the ED with shock will be discharged home (acknowledging rare, individualized circumstances, such as a patient who is on home hospice, etc.).

The majority of patients presenting with shock will require higher-level care and admission to an intensive care unit.

Summary

Shock is a catastrophic end result of circulatory collapse and inadequate cardiac output, characterized by end-organ hypoxemia, ischemia, and failure. There are numerous causes of shock, which are grouped into 4 distinct categories that are defined by common pathophysiologic mechanisms resulting in impaired delivery of oxygenated blood to peripheral tissues and organs. While the pathophysiologic

mechanisms of distributive, obstructive, hypovolemic, and cardiogenic shock are distinct, they may result in similar initial presentations with end-organ damage and cardiocirculatory insufficiency. Hypotension is common, but not obligatory, for the diagnosis of shock. An initial approach to undifferentiated shock includes establishing vascular access, empiric volume resuscitation, and comprehensive diagnostic assessment to identify the etiology(ies) of shock to guide subsequent focused treatment. Adherence to evidence-based care of the specific cause(s) of shock can optimize a patient's chances of surviving this life-threatening clinical condition.

Case Conclusion

You rapidly determined that the patient was in shock. Although his blood pressure was within acceptable limits,

Pitfalls To Avoid In The Diagnosis And Management Of Shock

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6. **“She has a fever and hypoxemia. Her hypotension is probably due to sepsis from pneumonia.”**

Failure to consider obstructive shock on the differential diagnosis can lead to inappropriate clinical management, such as treating a pulmonary embolism with antibiotics. Maintaining a broad differential diagnosis and considering obstructive pathophysiologic causes of shock, when clinically appropriate, can lead to more rapid diagnosis and treatment.

7. **“I read that a hemoglobin of 7 gm/dL is the evidence-based transfusion trigger, so let's hold off on giving this hypotensive trauma patient blood.”**

While conservative transfusion thresholds are appropriate for critically ill patients without active hemorrhage, prompt resuscitation with blood products is critically important for patients presenting with hemorrhagic shock. Furthermore, the hemoglobin concentration will not reflect the degree of blood loss early in such a patient's presentation, obligating the emergency clinician to identify possible acute hemorrhage based on the patient's clinical circumstances.

8. **“Her mean arterial pressure of 50 mm Hg is probably just because she's pregnant.”**

Numerous physiologic changes occur during pregnancy, including increased cardiac output, increased heart rate, and decreased systemic vascular resistance. The decrease in systemic

vascular resistance usually results in a drop in the mean arterial pressure of 5 mm Hg to 10 mm Hg from normal prepregnancy levels. Mean arterial pressures < 60 mm Hg, however, should raise awareness of the possibility of pathophysiologic processes contributing to hypotension.

9. **“Let's try bilevel positive airway pressure and see if his pneumonia gets better after antibiotics.”**

Recognition of multiorgan system failure and hypotension from septic shock that requires early intubation and mechanical ventilation is critically important. Failure to intubate early in the course of care for critically ill patients in septic shock can perpetuate the cycle of impaired oxygen uptake, deficient oxygen delivery to peripheral tissues, and increased metabolic demand from increased work of breathing. Furthermore, recognizing that a patient's disease process will take days, rather than hours, to resolve prioritizes intubation above noninvasive mechanical ventilation.

10. **“I know how to treat sepsis: antibiotics, fluids and pressors. I don't need a protocol.”**

Aggressive, protocolized, and bundled clinical management of patients in septic shock results in improved initial resuscitation and improved patient outcomes. Adherence to institutional guidelines for the initial treatment of septic shock is an important component of the acute care of severe sepsis and septic shock.

he had clear clinical evidence of impaired end-organ perfusion as evidenced by altered mental status (impaired cerebral perfusion) and respiratory insufficiency. While you recognized the possibility of a cardiogenic process contributing to his presentation, the majority of the clinical data supported an infectious process (specifically, a right lower lobe pneumonia) resulting in a systemic inflammatory response and distributive pathophysiology due to septic shock. You administered a bolus of 30 mL/kg of lactated Ringer's. You requested a comprehensive laboratory panel be sent, including CBC, chemistries and renal function analyses, arterial blood gas, serum lactate concentration, and blood cultures. You ordered a chest x-ray to better characterize his presumptive pneumonia. Because the patient was in shock due to sepsis, you ordered empiric broad-spectrum antibiotics based on your hospital's antibiogram – in this case you elected to administer vancomycin 15 mg/kg (as the patient's renal function is not yet known) and cefepime 2 gm IV. Despite these interventions, his blood pressure progressively decreased in the setting of an increasing temperature and worsening oxygenation. Given his clinical deterioration, you made the decision to intubate him and initiate mechanical ventilation with low-tidal-volume ventilation. Then, you placed a left subclavian central venous line and initiated a continuous infusion of norepinephrine, titrated for a MAP goal of > 65 mm Hg. His laboratory studies demonstrated leukocytosis (WBC 27 x 10⁹/L), thrombocytopenia (90 x 10⁹/L), acute renal failure (creatinine 3.1 mg/dL), and a lactic acidosis (lactate 7.2 mmol/L, bicarbonate concentration of 16 mmol/L, and base excess of -10 mEq/L). After receiving high-quality, evidence-based care in the ED, he was admitted to the MICU in critical condition, but ultimately made a full and uneventful recovery.

In The March/April Issue of *EM Practice Guidelines Update*

The March/ April 2014 issue of *EM Practice Guidelines Update* reviews 2 recently updated practice guidelines on the diagnosis, treatment, and prevention of *Clostridium difficile* infection (CDI) in the ED: the 2013 guideline from the American College of Gastroenterology and the 2014 guideline from the European Society of Clinical Microbiology and Infectious Diseases.

Seth Gemme, MD and Brian Clyne, MD review these guidelines for applicability in the ED and answer these questions:

- How are “mild,” “moderate,” “severe,” and “severe-complicated” CDI defined?
- What are the most effective tests for CDI that can be used in the ED?
- Should the emergency clinician treat suspected CDI empirically while awaiting test results?
- What is the first-line medication choice for each type of CDI? Recurrent CDI?

All subscribers to *Emergency Medicine Practice* have free access to this online publication at www.ebmedicine.net/Cdiff, and each issue also includes 2 hours of CME. For more information on this publication and to see the full archive of *EM Practice Guidelines Update* issues, go to “[What Is EM Practice Guidelines Update All About?](http://www.ebmedicine.net/content.php?action=showPage&pid=94&cat_id=16)” or http://www.ebmedicine.net/content.php?action=showPage&pid=94&cat_id=16.

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Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study will be included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the authors, will be noted by an asterisk (*) next to the number of the reference.

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- In early shock, the carotid baroreceptors respond to decreased blood pressure by triggering an increase in sympathetic signaling, resulting in which of the following systemic effects?**
 - Increased systemic vascular resistance
 - Decreased heart rate
 - Decreased cardiac output
 - Increased respiratory rate
- All of the following are potential benefits of intubation and initiation of mechanical ventilation for patients in shock EXCEPT:**
 - Decreased work of breathing
 - Improved right ventricular preload
 - Airway protection
 - Decreased systemic oxygen consumption
- Which of the following is the most rapid, accurate, and easily reversible means of assessing a patient's fluid responsiveness?**
 - Central venous pressure
 - Pulmonary capillary wedge pressure
 - Passive leg raise with a cardiac output monitor
 - Transthoracic echocardiography

4. Which of the following is appropriate for initial acute volume resuscitation for a patient presenting with septic shock?
 - a. Albumin 5%
 - b. Hydroxyethyl starch 3%
 - c. Packed red blood cells
 - d. Lactated Ringer's

5. For patients presenting with shock after trauma, which is an appropriate step in management?
 - a. Maintain hypotension to reduce intracranial pressure if traumatic brain injury is suspected.
 - b. Initiate aggressive crystalloid resuscitation instead of blood to reduce the risk of blood transfusions.
 - c. Early plasma transfusion if patients are anticipated to need massive transfusion.
 - d. Immediate CT scan of the spine to evaluate for neurogenic shock.

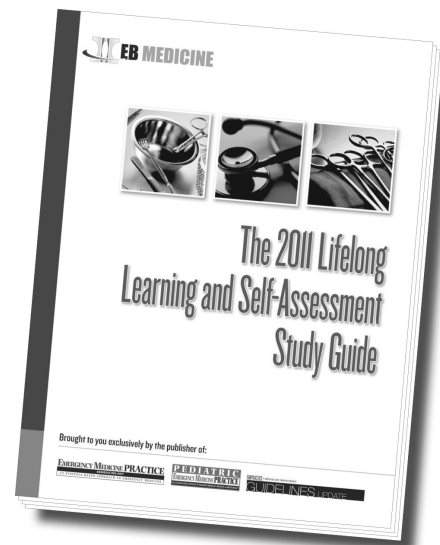
6. Which of the following should be performed very early in the presentation of a patient with septic shock?
 - a. Formal transthoracic echocardiography
 - b. Administration of broad-spectrum antibiotics
 - c. Pulmonary artery catheter placement
 - d. Noninvasive cardiac output monitoring

7. The 2012 update of the Surviving Sepsis Campaign recommends all of the following as appropriate initial interventions for patients presenting with septic shock EXCEPT:
 - a. Lactate should be checked at 0 and 6 hours.
 - b. Blood cultures should be drawn and broad-spectrum antibiotics given.
 - c. 30 cc/kg of crystalloid should be given for hypotension or lactate ≥ 4 mmol/L.
 - d. Packed red blood cells should be transfused if the hematocrit is $< 30\%$.

8. Mortality is decreased for patients with cardiogenic shock by which of the following interventions:
 - a. Early percutaneous coronary intervention within 90 minutes of presentation
 - b. Pulmonary artery catheter placement
 - c. Broad-spectrum antibiotics
 - d. A and B

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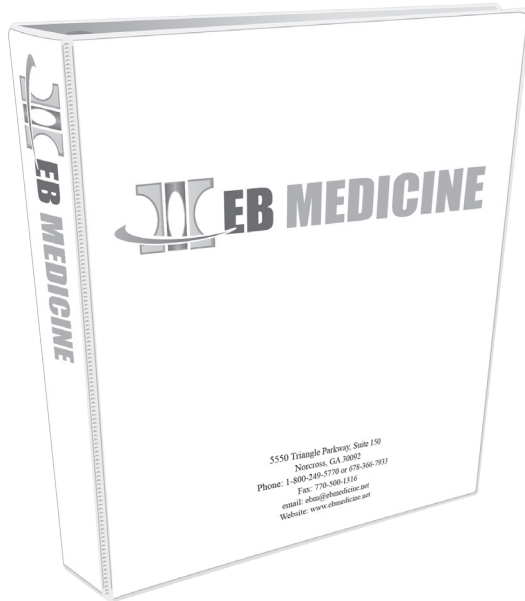
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